UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/671,316	09/24/2003	John Dwyer	TRM-002	2635

20583 7590 03/26/2008

JONES DAY
222 EAST 41ST ST
NEW YORK, NY 10017

EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
03/26/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/671,316	DWYER ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 17-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 17-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communication filed 13 December, 2007. Claims 1-8 and 17-24 are pending in the instant application.

35 U.S.C. § 112, Second Paragraph

The previous rejection of claims 1-8 and 17-24 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is hereby withdrawn in response to applicants' amendment and arguments.

35 U.S.C. § 103(a)

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4, 7, 8, 17, 20, 23, and 24, stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Bewley *et al.* (2002) in view of Ferrer *et al.* (1999). As previously set forth, Bewley *et al.* (2002) disclose synthetic peptides derived from the HR1 region of HIV-1 gp41 with potent antiviral activity. The peptides further comprised one or more amino acid

substitutions, including the designated heptadic positions (i.e., "e" or "f"). It was also demonstrated that these polypeptides form trimeric structures in solution and interact with the HR2 region of gp41. This teaching does not disclose a screening method to identify inhibitors of this binding interaction. However, Ferrer *et al.* (1999) disclose a screening method to identify small molecule inhibitors of HIV-1 cell fusion employing an HR1/HR2 binding assay. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to utilize the screening regimen of Ferrer *et al.* (1999), in the peptide binding assay of Bewley *et al.* (2002), to identify putative small molecule inhibitors of HIV-1 fusion. Both a reasonable expectation of success and the motivation to do so were clearly present in the prior art.

Applicants traverse and submit the claim amendments distinguish from the prior art. It was also argued that any attempt to arrive at the claimed invention would have been "obvious to try". Applicants' arguments have been carefully considered but are not deemed to be persuasive. First, it has been well-established in the art that the HR1 region (which comprises N36) forms a trimeric structure *in vitro* and *in vivo* that is required for virion-cell fusion. It has also been well-established that the HR2 region binds to said HR1 region during the fusion process. This has provided the basis for the design of both HR1 ($N36^{Mut}$) and HR2 (C34/T20 or DP178) inhibitors. Both Bewley *et al.* (2002) (Figure 1a, p. 14239) and Ferrer *et al.* (1999) (Figure 2, p. 954) disclose this binding interaction and *in vitro* antiviral screening assays that take advantage of it. Bewley and colleagues further disclose the heptadic repeat

structure of both the HR1 and HR2 regions and identify those portions of the heptadic repeat that interact with one another (see Figure 2., p. 14240). Although the HR1 polypeptides disclosed by Bewley and associates were precisely 36 amino acids in length, Ferrer and colleagues provide HR1 polypeptides that were ~49 aa in length. Moreover, it has been well-documented that HR1 extends from aa 543-600 (see background information provided by applicants and references relied upon). Thus, one of ordinary skill in the art would have been motivated to use polypeptides derived from this region. To ascertain the precise length employed would simply require routine experimentation. Moreover, numerous HIV-1 isolates were available in the prior art at the time of filing, thus it would have been prima facie obvious to employ HR1 regions from different isolates, to assess the ability of any given inhibitor to act on different clades.

Claims 2, 3, 5, 6, 18, 19, 21, and 22, stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Bewley *et al.* (2002), in view of Ferrer *et al.* (1999), as applied *supra* to claims 1, 4, 7, 8, 17, 20, 23, and 24, and further in view of Barney *et al.* (1999). As set forth *supra*, Bewley and colleagues disclose synthetic peptides derived from the HR1 region of HIV-1 gp41 with potent antiviral activity. The peptides further comprised one or more amino acid substitutions, including the designated heptadic positions (i.e., "e" or "f"). It was also demonstrated that these polypeptides form trimeric structures in solution. This teaching does not provide mutations in other regions of the heptadic repeat (i.e., "a", "d", or "b") or various modifications to the polypeptide (i.e., the addition of reactive groups or carriers). Ferrer *et al.* (1999) disclose a screening method to identify small molecule inhibitors of HIV-1

cell fusion employing an HR1/HR2 binding assay. Barney and associates provide similar polypeptides with enhanced pharmacokinetic properties. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the synthetic peptides of Bewley *et al.* (2002), as described by Barney *et al.* (1999), since this would produce synthetic polypeptides with enhanced pharmacokinetic profiles. Moreover, one of ordinary skill in the art would have been motivated to make "conservative" substitutions in other portions of the heptadic repeat (i.e., "a", "d", or "b") since structurally similar polypeptides would reasonably be expected to have similar activities.

Applicants are reminded that a *prima facie* case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. See M.P.E.P. 2144.09. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313, 203 U.S.P.Q. 245, 254 (C.C.P.A. 1979). See *In re Papesch*, 315 F.2d 381, 137 U.S.P.Q. 43 (C.C.P.A. 1963) (discussed in more detail below) and *In re Dillon*, 919 F.2d 688, 16 U.S.P.Q.2d 1897 (Fed. Cir. 1991) (discussed below and in M.P.E.P. § 2144) for an extensive review of the case law pertaining to obviousness based on close structural similarity of chemical compounds. See also M.P.E.P. § 2144.08, paragraph II.A.4.(c). Compounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus) or homologs (compounds differing regularly by the successive addition of the

same chemical group, e.g., by -CH2- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 563 F.2d 457, 195 U.S.P.Q. 426 (C.C.P.A. 1977). See also *In re May*, 574 F.2d 1082, 197 U.S.P.Q. 601 (C.C.P.A. 1978) (stereoisomers *prima facie* obvious).

Applicants again traverse and submit the claim amendments distinguish from the prior art. It was also argued that any attempt to arrive at the claimed invention would have been "obvious to try". Applicants' arguments have been carefully considered but are not deemed to be persuasive. First, it has been well-established in the art that the HR1 region (which comprises N36) forms a trimeric structure *in vitro* and *in vivo* that is required for virion-cell fusion. It has also been well-established that the HR2 region binds to said HR1 region during the fusion process. This has provided the basis for the design of both HR1 ($N36^{Mut}$) and HR2 (C34/T20 or DP178) inhibitors. Both Bewley *et al.* (2002) (Figure 1a, p. 14239) and Ferrer *et al.* (1999) (Figure 2, p. 954) disclose this binding interaction and *in vitro* antiviral screening assays that take advantage of it. Bewley and colleagues further disclose the heptadic repeat structure of both the HR1 and HR2 regions and identify those portions of the heptadic repeat that interact with one another (see Figure 2., p. 14240). Although the HR1 polypeptides disclosed by Bewley and associates were precisely 36 amino acids in length, Ferrer and colleagues provide HR1 polypeptides that were ~49 aa in length. Moreover, it has been well-documented that HR1 extends from aa 543-600 (see background information provided by applicants and references relied upon). Thus, one

of ordinary skill in the art would have been motivated to use polypeptides derived from this region. To ascertain the precise length employed would simply require routine experimentation. Moreover, numerous HIV-1 isolates were available in the prior art at the time of filing, thus it would have been prima facie obvious to employ HR1 regions from different isolates, to assess the ability of any given inhibitor to act on different clades.

Claims 1-8 and 17-24 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Chan *et al.* (1997) in view of Barney *et al.* (1999) and Ferrer *et al.* (1999). As previously set forth, Chan and colleagues disclose synthetic peptides derived from the HR1 region of HIV-1 gp41 with potent antiviral activity. This teaching does not provide mutations in other regions of the heptadic repeat (i.e., "a", "c", "d", or "b") or various modifications to the polypeptide (i.e., the addition of reactive groups or carriers). Barney and associates provide similar polypeptides with enhanced pharmacokinetic properties. Finally, Ferrer *et al.* (1999) disclose a screening method to identify small molecule inhibitors of HIV-1 cell fusion employing an HR1/HR2 binding assay. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the synthetic peptides of Chan *et al.* (1997), as described by Barney *et al.* (1999), since this would produce synthetic polypeptides with enhanced pharmacokinetic profiles. Moreover, one of ordinary skill in the art would have been motivated to make "conservative" substitutions in other portions of the heptadic repeat (i.e., "a", "c", "d", or "b") since structurally similar polypeptides would reasonably be expected to have similar activities. One of ordinary skill in the art would have also been motivated to use

these peptides in an HR1-HR2 binding assay to identify small molecule inhibitors of HIV-1 fusion as disclosed by Ferrer *et al.* (1999).

Applicants are reminded that a *prima facie* case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. See M.P.E.P. 2144.09. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313, 203 U.S.P.Q. 245, 254 (C.C.P.A. 1979). See *In re Papesch*, 315 F.2d 381, 137 U.S.P.Q. 43 (C.C.P.A. 1963) (discussed in more detail below) and *In re Dillon*, 919 F.2d 688, 16 U.S.P.Q.2d 1897 (Fed. Cir. 1991) (discussed below and in M.P.E.P. § 2144) for an extensive review of the case law pertaining to obviousness based on close structural similarity of chemical compounds. See also M.P.E.P. § 2144.08, paragraph II.A.4.(c). Compounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus) or homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH2- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 563 F.2d 457, 195 U.S.P.Q. 426 (C.C.P.A. 1977). See also *In re May*, 574 F.2d 1082, 197 U.S.P.Q. 601 (C.C.P.A. 1978) (stereoisomers *prima facie* obvious).

Applicants again traverse and submit the claim amendments distinguish from the prior art. It was also argued that any attempt to arrive at the claimed invention would have been "obvious to try". Applicants' arguments have been carefully considered but are not deemed to be persuasive. First, it has been well-established in the art that the HR1 region (which comprises N36) forms a trimeric structure *in vitro* and *in vivo* that is required for virion-cell fusion. It has also been well-established that the HR2 region binds to said HR1 region during the fusion process. This has provided the basis for the design of both HR1 ($N36^{Mut}$) and HR2 (C34/T20 or DP178) inhibitors. Chan and associates (1997) clearly disclose this binding interaction (see Figure 1, p. 264). Further structural studies were performed wherein various mutations were made to the heptadic repeat including positions a-e. Barney and colleagues (1999) provided numerous polypeptidic variants and Ferrer and coworkers (1999) provided an HR1 trimeric-HR2 monomeric drug screening assay. Clearly the invention is *prima facie* obvious in light of these teachings.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement

The previous rejection of claims 1-8 and 17-24 under under 35 U.S.C. § 112, first paragraph, because the specification does

not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, is hereby withdrawn upon further review of the prior art and applicants' arguments.

New Matter

Claims 1-8 and 17-24 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). The claims have been amended to incorporate the limitation "more than 36 amino acid residues" in reference to the size constraints associated with HR1 polypeptides. Perusal of the disclosure failed to provide support for the claimed limitation. The specification discusses HR1 polypeptides that are "no less than 16 and no more than 60 amino acids" (p. 13) and "no less than about 18 amino acids and no more than about 60 amino acid residues in length, and preferably no less than 30 amino acids and no more than about 51 amino acids in length, and more preferably no less than about 41 amino acids and no more than about 51 amino acids" (p. 17). However, support for the specific limitation "more than 36 amino acid residues" was not readily manifest.

Action Is Final, Necessitated by Amendment

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS**

ACTION IS MADE FINAL. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Bruce R. Campell, Ph.D., can be reached at (571) 272-0974. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence,

and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

/Jeffrey S. Parkin, Ph.D./

Primary Examiner, Art Unit 1648

23 March, 2008